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REPLY BRIEF

Pursuant to 37 C.F.R. § 41.41, Applicant responds to the Examiner's Answer as follows.

The prosecution of this application has been long and complicated, as is reflected by the length of this Reply Brief. The length of the prosecution, and this paper, particularly with regard to the issue of written description, the sole issue in this appeal, should not, however, suggest that this is in any way a close case. It is not a close case. The specification explicitly and implicitly describes the disputed claim term. In particular the Appellant asks that the Board not lose sight of the following: the specification explicitly recites the disputed claim term, so adding it is not new matter. In addition, the specification discloses a representative number of species for the genus represented by the disputed claim term. On these grounds (and other discussed herein) there is support for the disputed claim term. Nothing in the PTO's numerous arguments have shown otherwise.

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Applicant turns now to the grounds of rejection and arguments.

**(6) Grounds of Rejection/Arguments**

**Written Description/New Matter**

As set out in the Brief on Appeal, the sole issue on appeal is whether there is written description support for the following claim term, which is directed to an antibody, or antigen binding portion thereof, which:

> competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody

This claim term is sometimes referred to herein as the "disputed claim term," the "disputed class of competing antibodies," the "disputed class of antibodies" or similar terms.

Before addressing the arguments in the Examiner's Answer, Appellant first briefly summarizes its position and the arguments made in the Brief on Appeal and points out some differences between the PTO's argument as made in the Advisory Action Before the Filing of an Appeal Brief (referred to herein as the Advisory Action) and the Final Office Action and the arguments made in the Examiner's Answer. In essence, Appellant argued that the specification provides explicit and implied written description support for the disputed claim term. Arguments for explicit support are found at pages 4-14 of the Brief on Appeal. Arguments for implicit support can be found at pages 4-5 and 14-18 of the Brief on Appeal. These are independent arguments. Either can demonstrate adequate written description support for the disputed claim term. Appellant need only prevail on one of these arguments to show written description. These arguments are summarized very briefly below. The Board is directed to the Brief on Appeal for more detailed argument.

The specification provides explicit support for the disputed claim term

The plain language of the specification explicitly describes the disputed class of competing antibodies. See, e.g., page 27, line 26, through page 28, line 6, of the specification, which provides:

> In a particularly preferred embodiment of the present invention, a first biological agent[1] is conjugated with a prodrug which is activated only when in close proximity with a prodrug activator. The prodrug activator is conjugated with a second biological agent **according to the present invention**, preferably one which binds to a non-competing site on the prostate specific membrane antigen molecule. Whether two biological agents bind to **competing** or non-competing binding sites can be determined by conventional competitive binding assays. For example, monoclonal antibodies J591, J533, and E99 bind to **competing** binding sites on the prostate specific membrane antigen molecule. Monoclonal antibody J415, on the other hand, binds to a binding site which is non-competing with the site to which J591, J533, and E99 bind.
> (emphasis added)

The cited passage discusses a particular use of anti-PSMA antibodies of the invention, namely as targeting agents in a prodrug system. The passage considers two classes of antibodies of the invention, competing and non-competing, in its discussion of prodrug systems and their manufacture. It provides that non-competing antibodies are preferred for prodrug systems. The quoted passage also teaches how one can test antibodies to determine if they are in the competing class or the non-competing class, and provides working examples of competing and non-competing pairs of antibodies. All that remains is to show support for the disputed claim term is that the antibody "according to the invention" referred to in the cited language above can be one of the antibodies recited in the claims, namely E99, J415, J591 or J533. In other words to show that the antibody competed against is one of E99, J415, J533 and J591. This is shown by the fact that antibodies E99, J415, J533 and J591 are disclosed in the quoted passage and throughout the

[1] Biological agents are discussed as follows at page 13, lines 14-19 of the specification, "The process involves providing a biological agent, such as an antibody or binding portion thereof, probe, or ligand, which binds to an extracellular domain of prostate specific membrane antigen of (i.e., a portion of prostate specific membrane antigen which is external to) such cells."

specification as being antibodies of the invention. They are the only species described in the specification.

Thus, this passage recognizes and names the disputed class of competing antibodies. It provides representative working examples of antibodies in the disputed class of competing antibodies, and tells how to distinguish the disputed class of competing antibodies from the class of non-competing antibodies (which are said in the specification to be "preferred" in a prodrug system). The disputed class of competing antibodies is clearly recognized and shown to be in the possession of the applicant. The effort the inventor went to in order to characterize the two different classes of antibodies, to make representative working examples, and to explain how they are recognized shows that the inventor was in possession of the concept of competing antibodies. Appellant's position is that the disputed competing class is described and the description exists independently of which class is preferred to be incorporated, or can be incorporated, into the prodrug system. In the case of the preferred prodrug system, antibodies are tested to determine if they are in the disputed class, and if they are, they are set aside and not used in the preferred prodrug system. They still exist and the specification still provides written description of them.

In the Final Office Action and the Advisory Action the PTO argued that this class of antibodies was not described in the specification.[2] The PTO's position ignored the express language, the discussion of how one identifies the disputed class, and the specific working examples of the disputed class.

[2] In the Advisory Action the PTO's position appeared to be that the addition of the disputed claim term was prohibited on the grounds that the term itself represented new matter. In the Examiner's Answer the ground of rejection has changed. The PTO now appears to be alleging a lack of representative species. This is discussed in more detail below in the section which addresses the remarks made in the Examiner's Answer.

The PTO's position on written description may be explained, at least in part, by its incorrect view on the law on written description. See, e.g., the paragraph that bridges page 3, first full paragraph, of the Advisory Action:

> Applicants further refer to several court decisions: **in Re Smith, Purdue Pharma v. Faulding, Inc.,** and **In re Wright** which, taken out of context, appear to conclude that the original disclosure need not provide literal support or exact wording for claimed subject matter.
> (italics and bold typeface in the original, underlining added)

One must conclude from the quoted text that the rejection is based, at least in part, on the view that the case law requires "literal support or exact wording for claimed subject matter" and that only by taking the cases "out of context" can one come to the conclusion that literal or exact support is not required. This erroneous view of the law permeates both the Advisory Action and the Examiner's Answer. The Brief on Appeal, (see page 6) pointed out that this is erroneous. While this is certainly not the only flaw in the analysis, this misunderstanding, i.e., that express support must be literal or exact (i.e., in haec verba), permeates the analysis in both the Advisory Action and the Examiner's Answer and is one of the factors that contributes to the erroneous conclusion that the specification lacks written description for the disputed claim term.

The analysis in the Advisory Action also relies on the argument that prodrug/activator systems made with competing antibodies will not work and therefore the disputed class of competing antibodies is not described. See page 4 of the Advisory Action. The analysis confuses the utility or enablement of a prodrug/activator system (which is not the subject of the claims) with written description of two classes of antibodies, competing and non-competing, the second of which is preferred for use in the prodrug system.[3] The analysis assumes that a prodrug/activator system which uses competing antibodies will not work or could not be made to

[3] In the Examiner's Answer, the PTO appears to have modified its position on this point as well. The PTO now argues that the enablement arguments are relevant to how one of ordinary skill would read the specification. In the Examiner's Answer, the argument is that a competing antibody will not work in a prodrug system and since it would not work one of ordinary skill would not think the specification discloses it. This, and related issues, are discussed in more detail below in the section which addresses the remarks made in the Examiner's Answer.

work without undue experimentation. Even if that were true (and as set out at pages 11-12 of the Brief on Appeal it is not), it would go to the issue of whether claims to a prodrug/activator system made with competing antibodies would have utility or would be enabled, and not to the issue of whether there is written description for the disputed class of antibodies (not prodrug conjugates) discussed in the process of making the prodrug conjugate. The disputed class of antibodies has existence independent of being coupled to the prodrug. The invention is not a prodrug system but a genus of competing antibodies.

In essence, the PTO argument in the Advisory Action was as follows,

(a) the cited passage refers only to conjugates (and apparently not in the view of the Examiner to an antibody not conjugated to a prodrug),

(b) that competing antibodies won't work in a prodrug system, and

(c) thus, there is no written description for competing antibodies.

In Brief on Appeal, Appellant first, and independent of the additional arguments, maintained its position that competing antibodies are described, quite regardless of whether a prodrug system using competing antibodies is enabled. Even if competing antibodies would not be workable in a prodrug system that does not negate the possession of the concept of a class of competing antibodies. It is clear from the literal words of the specification that Appellant was in possession of the disputed class of competing antibodies, even though it provides that it is preferable to use non-competing in a prodrug system. Preference for the class of non-competing antibodies doesn't reverse, undo or negate the possession of the less preferred disputed class of competing antibodies.

Even if the PTO is correct and a competing antibody would not work in a prodrug system, the explicitly named and exemplified class that one is to avoid in constructing the antibody/prodrug conjugate is still described.

Second, and independent of the first argument, Appellant additionally pointed out that the PTO had not even shown the first premise of its argument, namely, that competing antibodies would not work, see pages 11-12 of the Brief on Appeal.

The specification provides implicit support for the disputed claim term

Appellant's second, independent, ground for finding written description support for the disputed claim term is "implicit support." In other words, even if one (improperly) ignored the fact that the class of competing antibodies was expressly discussed in the specification, the specification provides implicit recognition of the disputed class from the disclosure. The Brief on Appeal relied on relevant sections of the MPEP and cases cited therein which address the issue of support for a sub-genus from a species and/or generic disclosure. Appellant argued that application of the principles set out in the MPEP, and in the cases cited therein, to the facts of the instant matter require a finding of implicit support for the disputed claim term.

We turn now to specific arguments made in the Examiner's Answer.

On page 3, last full paragraph, of the Examiner's Answer, the Examiner characterizes a declaration provided by the Appellant as follows:

> Appellants further provided a Declaration by Abbie Celniker under 37 CFR 1.132 which proposes that the specification, on page 27, lines 26-35, indicates the Appellant was in *possession* of antibodies that compete with antibodies that compete for binding with J415, J591, J533 or E99.
> (emphasis in the original)

The declaration sets out Dr. Celniker's long and extensive experience with antibodies. She has been involved in the development of antibody-based projects in industry since at least 1986 and is currently Senior Vice President or R&D Strategy and Operations at Millennium Pharmaceuticals, Inc., the exclusive licensee of the above reference patent application. In her declaration, she provides as follows:

8. I want to be clear that I am not saying merely that the text makes it obvious to arrive at "antibodies or portions thereof that compete for binding to PSMA with monoclonal antibodies E99, J415, J533 and J591" or that the specification discloses a general concept of what antibodies might compete and that it is only obvious that these would be E99, J415, J533 and J591. On the contrary, it is clear to me that, upon reviewing the specification of the above-referenced application, one of ordinary skill in the art at the time the application was filed, would have believed that the text itself describes and actually shows possession of the subject matter in question. It is really a rather simple matter: a series of consecutive sentences in the specification build on one another and require this conclusion. I have summarized the situation below, where the relevant text (e.g., page 27, line 26, through page 28 line 6) is presented in annotated form:

| Text from the specification | Meaning |
|---|---|
| In a particularly preferred embodiment of the present invention, a first biological agent is conjugated with a prodrug which is activated only when in close proximity with a prodrug activator. (page 27, lines 26-29) | These two sentences tell one of ordinary skill that the applicant was in possession of antibodies which compete with antibodies of the invention and give the meaning of the term compete for binding. |
| The prodrug activator is conjugated with a second biological agent according to the invention, preferably one which binds to a non-competing site on the prostate specific membrane antigen molecule. Whether two biological agents bind to competing or non-competing binding sites can be determined by conventional competitive binding assays. (page 27, lines 29-35) | |
| For example, monoclonal antibodies J591, J533, and E99 bind to competing binding sites on the prostate specific membrane antigen molecule. Monoclonal antibody J415 on the other hand, binds to a binding site which is non-competing with the site to which J591, J533, and E99 bind. (page 28, lines 1-6) | This sentence, the next sentence in the specification, tells one that the specific antibodies mentioned in the claim (J415, J591, J533 and E99) are antibodies of the invention. |

> Thus, one reading this passage, learns from the first four sentences that antibodies which compete for binding with antibodies of the invention are described. A few lines later one learns that J415, J591, J533 and E99 are antibodies of the invention. It is simply inescapable that the specific examples of antibodies of the invention, J415, J591, J533 and E99, provided in the text can be placed in the context of the earlier sentence. It is clear to me that, upon reviewing the specification of the above-reference application, one of ordinary skill at the time the application was filed, would have believed that the specification discloses, and the inventors were in possession of, antibodies that compete for binding with the listed antibodies, in other words, antibodies that compete for binding with one or more of J415, J591, J533 or E99.
>
> (emphasis in the original)

The PTO never provides reasoned grounds for why Dr. Celniker's conclusion of what one of ordinary skill in the art would think the specification conveys should not be accepted.

In the first sentence of the second paragraph on page 4 of the Examiner's Answer, the PTO asserts that Appellant argues that it is "in possession of all such competing antibodies." Appellant argues that the specification provides written description support of the disputed class of competing antibodies and numerous species in it but has never argued it is in possession of all possible antibodies within the genus.

In the paragraph that bridges pages 4 and 5, the Examiner's Answer appears to concede that the much discussed passage of the specification (the passage from page 27, line 26, through page 28, line 6, of the specification, reproduced herein on page 3) "may not necessarily exclude the use of competing antibodies." The Examiner's Answer then goes on to take a new position, and, as alluded to earlier herein, makes an argument not previously made in this case, namely that the specification fails to "fully described the scope of the claims."

See the section which bridges pages 4 and 5 of the Examiner's Answer:

> Although this particular passage may not necessarily exclude the use of competing antibodies, the issue is whether or not Appellants have fully described the scope of the claims; a subgenus of antibodies that compete for binding to PSMA with the species of monoclonal antibodies—E99, J415, 533, and J591. In this particular case, the written description requirement for the claimed genus of antibodies that bind to the extracellular domain of PSMA are satisfied through sufficient description of a representative number of the latter species of monoclonal antibodies. However, the same cannot be said for the clamed "subgenus" of antibodies because Appellants have not identified a representative number of species that adequately describe the entire subgenus.

Thus, one sees, for the first time in the prosecution of this case, the argument that sufficient species are not provided. The substance of the new argument begins in the second sentence of the text just quoted, where the PTO argues that the specification does provide a sufficient number of representative species to support a much broader genus namely "the claimed genus of antibodies that bind to the extracellular domain of PSMA."[4] Thus, the four species present in the specification are said to be sufficient for written description of a broad claim, a claim that covers any antibody which binds any epitope on the extracellular domain of PSMA. See the paragraph that bridges pages 4 and 5 of the Examiner's Answer:

> In this particular case, the written description requirement for the claimed genus of antibodies that bind to the extracellular domain of PSMA are satisfied through sufficient description of a representative number of the latter species of monoclonal antibodies.

However, in the next line of the Examiner's Answer, the PTO takes the position that the very same species fail to support written description for a much narrower genus. This is wrong, particularly in view of the fact that all[5], of the species in question also fall within the much

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[4] Appellant notes that the genus referred to in the Examiner's Answer as "the claimed genus" is in fact not claimed.
[5] Monoclonal antibodies E99, J415, J533, or J591, are the antibodies which define the breadth of the claim, in other words, to be within the claim, an antibody must compete with one of these four antibodies for binding to PSMA. Each of these four antibodies is also a species within the claim as each is capable of competing with at least one of

narrower subgenus. The disclosed species are said to support the broad claim--there is absolutely no reason to believe that the disclosed species would not be representative of the narrower claim. Logically, if they are representative of the broad claim, they are representative of the narrower claim, absent some compelling argument to the contrary (which argument is conspicuous in its absence).

The fallacy in the PTO's position on representative species is evident when one turns to the arguments on exactly what parameters of the species are said to show substantial variation. See page 5 of the Examiner's Answer:

> Further, antibodies that encompass the subgenus of "competing" antibodies would include substantial variation because the disclosed species of antibodies (i.e., E99, J415, J533, and J591) include those that bind to different epitopes on the PSMA molecule. Furthermore, competing antibodies could include any antibodies that hinder binding such as those that differ in size. Thus, it cannot be said that one of ordinary skill in the art would recognize (either implicitly or explicitly) that Appellants were in possession of the claimed subgenus because the disclosure fails to describe a sufficient variety of species to reflect the variation within the subgenus.

The Examiner's Answer provides argument that two parameters are subject to substantial variation: the epitopes bound by antibodies in the subgenus; and, the size of the antibodies in the subgenus. Neither argument holds up.

Appellant turns first to the variation of epitope. The subgenus includes only antibodies that compete for a very small number of epitopes (those characterized by competition with the four disclosed species). This does not represent a level of variation that would deprive the term of written description support. It is very difficult to see how the variation among species of the disputed class, a subgenus (i.e., an antibody that competes with E99, J415, J533, or J591), would be greater than the variation in epitope seen among the species in the broader genus (an antibody that binds <u>any</u> epitope of the extracellular domain of PSMA), which broader genus was found by

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the four defining antibodies. E99 can compete with itself, J533, and J591. J533 can compete with itself, E99, and J591, and so on.

the PTO to have been sufficiently described. After all, the subgenus includes only antibodies that compete for binding with antibodies to a very small number of epitopes (four at the most). The broader genus, admitted by the PTO to be sufficiently described, includes any antibody that binds anywhere to any epitope on the extracellular domain of PSMA. The broad genus, with its vastly greater level of variation was (correctly) found by the PTO to satisfy the written description requirement, thus the disputed subgenus must also satisfy the written description requirement, absent some compelling argument to the contrary (which argument is conspicuous in its absence).

The Appellant's position is also supported by the PTO's Written Description Guidelines (referred to herein as the "Guidelines"). The Guidelines provide a decision tree and analytical framework for determining if there is written description support for a genus. See the "Genus Analysis" decision tree in the Guidelines. According to the Guidelines, the first step is to:

> Determine whether the art indicates substantial variation among the species within the genus of the claimed subject matter.
>
> The next step requires the following analysis:
>
> Is there a representative number of species implicitly or explicitly disclosed? What is a representative number of species depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species

The Guidelines then apply the analysis to the facts presented in an example which deals with antibodies (Example 16). In Example 16, the specification provides a well described antigen and "contemplates" an antibody but provides no working examples. In the analysis of Example 16 the Guidelines state:

> The general knowledge in the art is such that antibodies are structurally well characterized. It is well known that all mammals produce antibodies and they exist in five isotypes, IgM, IgG, IgD, IgA and IgE. Antibodies contain an effector portion which is the constant region and a variable region that contains the antigen binding sites in the form of complementarity determining regions and the framework regions. The sequences

> of constant regions as well as the variable regions subgroups (framework regions) from a variety of species are known and published in the art. It is also well known that antibodies can be made against virtually any protein.
>
> ...
>
> Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Thus, the Guidelines found that a specification which disclosed a well characterized antigen but which completely lacked any examples provided written description for the genus of antibodies which bind to the antigen. The Guidelines acknowledge that the high degree of skill in the art with regard to antibodies and the known common structural functional attributes of antibodies provide for a sufficient written description of a genus of antibodies where the antigen is well characterized but no specific examples are provided. In the instant matter, the antigen, PSMA, is well characterized. In addition, the antibodies against which the antibodies of the invention must compete are exceptionally well characterized—those antibodies, E99, J415, J533, or J591, were provided as working examples in the specification (and deposited, see page 31 of the specification).[6] Thus, the specification meets, and indeed exceeds, what is required by the Guidelines.

Appellant turns now to the only other parameter said by the PTO to exhibit substantial variation--antibody size. It is difficult to see how the variation in size among species of the disputed class, a subgenus (antibodies that compete with E99, J415, J533, or J591), would be greater than that seen in the variation in size among the species in the broad genus (antibodies that binds to any epitope of the extracellular domain of PSMA). The broader genus, found by the Examiner to be described, would by definition include more antibodies, and would, if anything have the potential for greater variation in size. There is no reason to believe that the variation of species in the disputed class of antibodies would exhibit variation so substantial as to

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[6] See footnote 5.

deprive it of written description. The Appellant's position is also supported by the Guidelines. The structure (which includes size) of the various types of antibodies was explicitly taken into account in the analysis of antibodies in Example 16 of the Guidelines and found not to be an issue for written description, even in a specification that provided no working example and which said nothing about size. Thus, the disclosed species are representative of the disputed class of competing antibodies.

In the last paragraph on page 5, the Examiner's Answer turns to arguments about misinterpretation or misapplication of the law:

> Appellants further argue (Brief, page 12) that the rejection is based on a misapplication of the law because it relies heavily on the argument that prodrug/activator systems made with competing antibodies will not work. Appellants argue that this analysis confuses the "utility or enablement of a prodrug/activator system (which is not the subject of the clams) "with written description of the antibody components used to make the prodrug/activator system. This argument has been considered but is not found persuasive because Appellant's alleged support of the subgenus invited uncertainty. Further it is not understood how the Examiner's response was misapplied because the statue underlying the first paragraph of 35 USC 112 includes issues regarding enablement and written description. Moreover, the courts appear to have indicated that operability is related to a complete disclosure. See MPEP 2163.05: A patentee will not be deemed do have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other that the one disclosed." In re Curtis, 345 F.3d 1347, 1358, 69 USPQ2d 1274 (Fed. Cir. 2004)

Appellant first provides the context of this argument and will then address the various elements of this passage. Appellant's position is that the disputed class of competing antibodies is described regardless of the level of preference and regardless of whether a prodrug system which uses competing antibodies would work. The PTO ignored the express description of the class and the working examples of species within it and argued that prodrug conjugates which include competing antibodies would not work. See page 4 of the Advisory Action. As discussed at pages 11-13 of the Brief on Appeal, that argument borrowed heavily from enablement and utility analysis.

In the Examiner's Answer, the PTO has modified its position on the relevance of enablement/utility--the PTO now argues that the enablement and utility language really went to its interpretation of the term "preferred." (That new argument will be discussed in its turn below.) But despite this new approach, the PTO has expressly admitted that its earlier approach relied on mixing enablement and written description and still argues for the validity of that analysis –i.e., it has not given up on the acceptability of directly confounding written description with enablement, see page 6, lines 5-7, of the Examiner's Answer:

> This argument has been considered but is not found persuasive because Appellant's alleged support of the subgenus invited uncertainty. Further, it is not understood how the Examiner's response was misapplied because the statue underlying the first paragraph of 35 USC 112 includes issues regarding enablement and written description

The Examiner's Answer, in direct conflict with both the MPEP and a considerable body of settled Federal Circuit case law, argues that because 35 USC 112 sets out the enablement and written description requirements in the same statutory section it is proper to use an analysis of enablement in a written description rejection.[7] This is incorrect. Written description and enablement (as well as best mode, which is also set out in this section of the title 35) are separate and distinct from one another. See, e.g., MPEP 2161, which provides, in pertinent part:

> The written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), *cert. denied*, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991)...An invention may be described without the disclosure being enabling (e.g., a chemical compound for which there is no disclosed or apparent method of making), and a disclosure could be enabling without describing the invention (e.g., a specification describing a method of making and using a paint composition made of functionally defined ingredients within broad ranges would be enabling for formulations falling within the description but would not describe any specific formulation). See *In re Armbruster*, 512 F.2d 676, 677, 185 USPQ 152, 153 (CCPA 1975) ("[A] specification which 'describes' does not necessarily also 'enable' one skilled in the art to make or use the claimed invention.").
> (emphasis added)

[7] Appellant notes that the rejection made and under appeal is a written description rejection.

The Examiner's Answer then presents further arguments to justify its analysis, again see page 6, first paragraph of the Examiner's Answer:

> Moreover, the courts appear to have indicated that operability is related to a complete disclosure. See MPEP 2163.05: A patentee will not be deemed do have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other that the one disclosed." In re Curtis, 345 F.3d 1347, 1358, 69 USPQ2d 1274 (Fed. Cir. 2004)

It is not clear if the PTO views this as a further justification of an enablement based analysis of written description (under the term operability) or supports an attack on based on lack of sufficient species. In either case, it is ineffective.

If this section of the MPEP is relied on as a further justification of an enablement-based analysis, the reliance is misplaced. Review of MPEP 2163.05 shows that it does not deal with enablement and in any event, as discussed above, enablement and written description can not be confounded. MPEP 2163.05 addresses the situation where there is no explicit written description for the genus[8] but the applicant argues that it has provided sufficient species disclosure to provide written description for a genus which encompasses them. This section of the MPEP says that a single species is not adequate when the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. So the connection to operability in this section of the MPEP is in the context of using a single species to support a genus. That is simply not relevant. Multiple species are disclosed in the specification. Furthermore, the Written Description Guideline shows that antibodies are a technology where the ordinary artisan could predict the operability of species other than the one disclosed. In fact the Guidelines, see Example 16 thereof, went even further than is needed to support Appellant's position. It found a genus was supported in the absence of any specific example—thus, in this technology one can predict the operability even with no working example.

If this section of the MPEP is relied on in the Examiner's Answer to mean that the species of non-competing antibody/prodrug conjugate is the only functional species and it is not

[8] This is in stark contrast to the facts of the instant case where the disputed term "competing" is found repeatedly in the text at page 27, line 26, through page 28, line 6,,of the instant specification.

predictable that the species of competing antibody prodrug conjugate would be operable that reliance is misplaced. The invention is an antibody not a conjugate. (Furthermore, as argued in detail in the Brief on Appeal, the PTO has not made the case that a conjugate made with a competing antibody is not enabled.)

Finally, even though Appellant's view is that this section of the MPEP, as relied on by the PTO, does not support the PTO's argument, Appellant never-the-less points out that the text of MPEP 2163.05 relied on in the Examiner's Answer was taken out of context. The Examiner's Answer reproduces a passage which fails to find support from a single species. It does not include the next few lines of that section of the MPEP. That text discusses cases where a single species did support a genus.

The next section of the Examiner's Answer, see last paragraph on page 6 through page 8, concerns the issue of whether the fact that non-competing antibodies are preferred in conjugates rules out the possibility that they can be used in antibody/prodrug conjugates. Again, Appellant's position is that this argument, even if correct, is irrelevant. The disputed class of competing antibodies was described even if only to be avoided. The PTO takes the position that because the specification says non-competing are preferred it means that competing cannot be used.

On page 7 of the Examiner's Answer, the PTO argues as follows to justify its restrictive definition of "preferred":

> In reviewing the phraseology, it was noted that the specification on page 27 disclosed "preferably one":
>
> > The prodrug activator is conjugated with a second biological agent according to the invention, preferably one which binds to a non-competing site on the prostate specific membrane antigen molecule.
>
> ...Thus, in reviewing this phrase, the Examiner took the position that "what is preferable" is that which one of ordinary skill in the art would commonly use or recognize in a prodrug/activator scenario, i.e., non-competing ligands, probes, or antibodies or fragments thereof. To suggest that this phrase also

> included "competing antibodies", from a scientific standpoint, seemed illogical and the Examiner provided reasoning as to why there did not appear to be support in this particular scenario...
> (emphasis in the original)

As alluded to above, the PTO has changed its arguments and also argues that the enablement/utility language relates to how one of ordinary skill in the art would interpret the term "preferred." None of this is persuasive. Regardless of the level of preference the disputed class was named and exemplified with representative working examples. The level of preference does not negate the express description provided in the specification at page 27, line 26, through page 28, line 6.

Furthermore, as set out in the Brief on Appeal at pages 111-12, the PTO has not shown that a competing antibody would not work. Thus, the core of the PTO argument has not been substantiated.

There is no support in the specification for the PTO's interpretation of the term "preferred." The ordinary meaning of the word also contradicts the definition the PTO needs for its argument. When one looks to dictionaries for the meaning of "preferable" or "preferably" one fails to find any support for the absolute meaning assigned to it by the PTO. Appellants surveyed three on-line dictionaries[9]—none of them equates preferred with "exclusively preferred" or "preferred to the exclusion of all else", which is the definition adopted by the PTO.

The Oxford English Dictionary, 2d edition, 1989, defines the adjectival form of "preferable" as follows (examples of usage have been omitted):

> 1. Worthy to be preferred; to be chosen before or desired rather than another; more desirable...
> †2. Displaying preference; preferential... *Obs.*
> 3. = preference 8. *attrib.* ...

Webster's Online Dictionary, the Rossetta Edition, copyright 2005: defines the adjectival form of preferable as

> 1. More desirable than another; "coffee is preferable to tea"; "Danny's preferred name is 'Dan'".

[9] The Oxford English Dictionary, 2d edition, 1989, Webster's Online Dictionary, the Rossetta Edition, copyright 2005, and Merriam Webster Online Dictionary, copyright 2005.

The same dictionary defines the adverb "preferably" as follows:

> 1. More readily or willingly; "clean it well, preferably with warm water"; "I'd rather be in Philadelphia"; "I'd sooner die than give up".

Merriam Webster Online Dictionary, copyright 2005, defines the adjectival form "preferable", as having greater value or desirability : being preferred.

None of the dictionaries consulted have the absolute sense relied on by the PTO. Preferred does not mean exclusive, in all of the definitions canvassed it merely means more preferred.

In the paragraph bridging the bottom of page 7 to the top of page 8, of the Examiner's Answer, the Examiner discusses the Declaration of Dr. Abbie Celniker. The argument ignores much of what is in the declaration (e.g., Dr. Celniker's reasoned argument that one of ordinary skill would understand that the specification conveyed possession of the disputed class of antibodies) and focused on the fact that non-competing antibodies were preferred in a prodrug system. There is really no issue about whether non-competing are preferred, they are preferred in that system, as is set out in the specification. However, it is just as clearly set out in the specification that there is another class of antibodies, namely competing antibodies, which regardless of how much less preferred they exist and need to be distinguished from non-competing antibodies in the preferred embodiment. The Examiner makes no argument here that hasn't already been made and addressed. The fact that non-competing is preferred does not negate possession of a less preferred class. In the case of the preferred prodrug system, antibodies are tested to determine if they are in the disputed class, and if they are, they are set aside and not used in the preferred prodrug system. They still exist and the specification still provides written description of them.

The Examiner's Answer turns next to Appellant's arguments with regard to implicit support for the disputed claim term, see pages 8-10 of the Examiner's Answer. The PTO's argument begins on the first full paragraph of page 9, where the use of terms such as "sub-

genus", "sub-sub-genus", "sub-generic" and "sub-sub-generic" is criticized. The Examiner's Answer provides as follows, on page 9, first full paragraph:

> On the one hand, Appellants inserted terms such as "sub genus", "sub-sub-genus", "sub-generic" and "sub-sub-generic' in describing the Board's opinion. However, none of these terms have "antecedent basis" in the actual written opinion established by the Board (see attached Board decision). The Board appears to have based their decision on the presence of working examples. For example, with regards to binuclear copper complexes of "aryl" and or "aliphatic" carboxylic acids, the board noted five working examples of binuclear copper complexes of carboxylic acids-four were "aryl" and one was "aliphatic". There is no recitation that these examples were member of a sub-sub-genus.

The Examiner's Answer argues that there is no "antecedent basis" for the terms used by appellant to describe claims of varying breadth and that the Board (referring to the decision in Ex parte Sorenson) based the "decision on the presence of working examples." One or both of these arguments is meant to distinguish the facts in the instant matter. Neither is persuasive.

The difference in terminology used to refer to claim elements of varying breadth in the Brief on Appeal and Ex parte Sorenson is meaningless. Despite the fact that the Brief on Appeal and Ex parte Sorenson use different terms or words to describe generic/subgeneric/species relationships they are both concerned with the same issue. Ex parte Sorenson was about determining whether a broad disclosure and the disclosure of several working examples could support claims of intermediate breadth. There were three claims of intermediate breath at issue. One claim term was narrower than the broad disclosure so Appellant referred to it as subgeneric (this was "binuclear copper complexes of carboxylic acids). Two claim terms (binuclear copper complexes of aryl carboxylic acids and binuclear copper complexes of alkyl carboxylic acids) were narrower than the subgenus, so Appellant referred to them as sub-sub generic. But regardless of what they were called, the principle is the same—was there support for the intermediate positions. In Ex parte Sorenson, the Board found five working examples, four of which were aryls and one of which was aliphatic. The four aryl working examples were found to support what Appellant referred to as the aryl sub-sub-genus and the one aliphatic example was found to support what Appellant referred to as the aliphatic sub-sub-genus. In Ex parte Sorenson

the terms "broad expression" and "narrower expression" were used. The choice of a particular terminology is simply not substantive.

Ex parte Sorenson, by its own terms and in the view of the MPEP (see below) is a case about inferring a subgenus from a broader genus together with one or more examples. That is what Appellant relied on it for. It is quite clear that the MPEP regards Ex parte Sorenson as dealing with the question of when a broader genus together with one or more species would support written description of a subgeneric position. See MPEP 2163.05(II) which provides, in pertinent part:

> While these and other cases find that recitation of an undisclosed species may violate the description requirement, a change involving subgeneric terminology may or may not be acceptable. Applicant was not entitled to the benefit of a parent filing date when the claim was directed to a subgenus (a specified range of molecular weight ratios) where the parent application contained a generic disclosure and a specific example that fell within the recited range because the court held that subgenus range was not described in the parent application. *In re Lukach*,. On the other hand, in *Ex parte Sorenson*, the subgeneric language of "aliphatic carboxylic acid" and "aryl carboxylic acid" did not violate the written description requirement because species falling within each subgenus were disclosed as well as the generic carboxylic acid.
> (emphasis added, citations omitted)

The MPEP uses terms such as generic, subgeneric, subgenus, and specific example (a species). The MPEP cites In re Lukach and Ex parte Sorenson as cases which have considered the issue of support for a term of intermediate breadth (subgenus or subgeneric) could be supported by broader (generic) and narrower (species) disclosure. Indeed, although the Examiner's Answer is troubled by the lack of the terms "generic", "subgeneric", "sub-sub-generic" in Ex parte Sorenson, the MPEP was not. Again, here is how the MPEP characterized Ex parte Sorenson:

> the subgeneric language of "aliphatic carboxylic acid" and "aryl carboxylic acid" did not violate the written description requirement because species falling within each subgenus were disclosed as well as the generic carboxylic acid.
> (emphasis added)

The exact same situation is presented by the instant case, do the working examples (and other generic disclosure) support a claim term of intermediate breadth. It really makes no difference if one refers to it in generic/subgeneric/example terminology or some other terminology. The principle is the same. The fact that the terms used by the Appellant (and the MPEP) did not appear in one of the two cases argued by the Appellant is simply irrelevant.

The argument in the Examiner's Answer also says "The Board appears to have based their decision on the presence of working examples." If the emphasis on "working example" (in contrast to "species", which might include a prophetic example) in the Examiner's Answer is meant to distinguish the instant matter, it does not. The species relied on in the instant matter are working examples.

The decision referred to, Ex parte Sorenson, was concerned with whether the intermediate subgenus had support—exactly the question which is being asked here. The argument in the Examiner's Answer may be emphasizing "working examples" (as opposed to species, which could be prophetic) to distinguish the instant case. That argument fails, as the instant case relies on working examples (and not prophetic examples) for its species. In addition, as discussed below, the MPEP characterized the case as relying on species. The MPEP finds that "species" (as opposed to working examples) is what was critical (see the passage form the MPEP quoted just above). But even if the MPEP did say working example, which it doesn't, the Examiner's argument fails as the species in the specification were actual working examples.

In the Brief On Appeal, see pages 15-18, Appellant provided a detailed comparison of the facts of the instant matter to those of In re Lukach and Ex parte Sorenson and of the application of the law to the facts of the instant matter. Appellant's argument showed there was implicit support for the disputed claim term. The substantive response to that discussion is limited to the following, see the paragraph which bridges pages 9 and 10 of the Examiner's Answer:

> While the four monoclonal antibodies represent species of the genus, they are not examples of species within the subgenus of 'antibodies that compete for binding with one of J591, E99, J415, and J533" because members of the subgenus have yet to be discovered or produced. They cannot include the known species of antibodies that bind to

> the extracellular domain of PSMA. Thus there is neither implict (sic) nor explicit support for the subgenus of antibodies that compete for binding to J591, E99, J415, and J533.

The crux of this argument seems to be that "members of the subgenus have yet to be discovered or produced." The Examiner's Answer has not provided any support for the fact that actual Examples would have to have been generated to have sufficient written description. But that does not really matter because the Examiner's Answer is simply wrong when it says examples have not been made. E.g., the claim covers antibodies which compete with J591—two of these, not counting J591 itself, have been produced, namely E99 and J533. The claim covers antibodies which compete with J533—two of these, not counting J533 itself, have been produced, namely E99 and J591. The claim covers antibodies which compete with E99—two of these, not counting E99 itself, have been produced, namely J591 and J533. So the Examiner's Answer is just plain wrong, members of the subgenus have been produced, even though as discussed above in the section on the Guidelines, actual examples are not required to support a generic antibody claim where the antigen is well characterized.

The Examiner's Answer concludes with a quote from In re Smith, "It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads." That may well be true but the MPEP and cases cited therein, such as, In re Lukach and Ex parte Sorenson provide guidance as to when a subgenus can be described by a genus and one or more species on which it reads. (Indeed in Ex parte Sorenson the Board found exactly that, namely that the subgenus of aliphatic molecules was supported by a genus and one example). Here the disputed subgenus is supported by more than a genus and a single example, as is described at pages 14-17 of the Brief on Appeal. Appellant has shown that application of the guidance provided in the MPEP and cases cited therein shows the specification provides implicit written description for the disputed class of competing antibodies.

For these reasons, and the reasons stated in the Appeal Brief, Applicant submits that the final rejection should be reversed. Appellant request removal of the rejections and remand of the case to the Examiner for allowance.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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